

**PRELIMINARY AMENDMENT**

Serial Number: 09/877,606

Filing Date: June 8, 2001

Title: ANTIGEN FOR DEVELOPING NEUTRALIZING ANTIBODIES TO HUMAN IMMUNODEFICIENCY VIRUS

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**In the Claims**

Please cancel claims 1- 47 without prejudice, and add claims 48-91 as follows:

48. (New) A stabilized viral envelope protein comprising three parallel,  $\alpha$ -helical COOH-terminal viral envelope glycoprotein monomers that together form a stable three-stranded coiled coil having a conformation like that of a native form of the viral envelope glycoprotein when associated with a cellular membrane, wherein the stabilized viral envelope protein is substantially incapable of undergoing a conformational change to become active for membrane fusion, and wherein the monomer comprises SEQ ID NO:8.
49. (New) The stabilized viral envelope protein of claim 48, wherein the native form of a viral envelope glycoprotein is an HIV1 or HIV2 viral envelope glycoprotein.
50. (New) The stabilized viral envelope protein of claim 48, wherein the native form of a viral envelope glycoprotein comprises three HIV gp41 monomers that form a trimeric coiled coil, in a prefusogenic conformation.
51. (New) The stabilized viral envelope protein of claim 48, wherein the monomer is recombinantly produced.
52. (New) The stabilized viral envelope protein of claim 48, wherein the monomer is synthetically produced.
53. (New) The stabilized viral envelope protein of claim 48, wherein the three-stranded coiled coil is stabilized by fusion of the monomer to an isoleucine zipper.

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54. (New) The stabilized viral envelope protein of claim 48, wherein the three-stranded coiled coil is stabilized by one or more point mutations.
55. (New) The stabilized viral envelope protein of claim 54, wherein the three-stranded coiled coil with one or more point mutations has SEQ ID NO:9.
56. (New) The stabilized viral envelope protein of claim 48, wherein the three-stranded coiled coil is stabilized by chemical cross-linking.
57. (New) The stabilized viral envelope protein of claim 50, wherein the gp41 monomers comprise SEQ ID NO:7.
58. (New) The stabilized viral envelope protein of claim 50, wherein the gp41 monomers comprise comprising SEQ ID NO:3 or SEQ ID NO:4.
59. (New) The stabilized viral envelope protein of claim 57 or 58, wherein a stable three-stranded coiled coil formed from the gp41 monomers is stabilized by chemical cross-linking.
60. (New) The stabilized viral envelope protein of claim 57 or 58, wherein a stable three-stranded coiled coil formed from the gp41 monomers is stabilized by one or more point mutations in one or more gp41 monomers.
61. (New) The stabilized viral envelope protein of claim 60, wherein the gp41 monomers with one or more point mutations comprise SEQ ID NO:9.
62. (New) A vaccine for the prevention or treatment of infection by an enveloped virus, said vaccine comprising a stabilized viral envelope protein comprising three parallel,  $\alpha$ -helical COOH-terminal viral envelope glycoprotein monomers that together form a stable three-stranded coiled coil having a conformation like that

needs  
additional  
components  
(e.g., adjuvant  
etc.)

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of a native form of the viral envelope glycoprotein when associated with a cellular membrane, wherein the stabilized viral envelope protein is substantially incapable of undergoing a conformational change to become active for membrane fusion, and wherein the monomer comprises SEQ ID NO:8.

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63. (New) The vaccine of claim 62, wherein the native form of a viral envelope glycoprotein is an HIV1 or HIV2 viral envelope glycoprotein.
64. (New) The vaccine of claim 62, wherein the native form of a viral envelope glycoprotein comprises three HIV gp41 monomers that form a trimeric coiled coil, in a prefusogenic conformation.
65. (New) The vaccine of claim 62, wherein the monomer is recombinantly produced.
66. (New) The vaccine of claim 62, wherein the monomer is synthetically produced.
67. (New) The vaccine of claim 62, wherein the three-stranded coiled coil is stabilized by fusion of the monomer to an isoleucine zipper.
68. (New) The vaccine of claim 62, wherein the three-stranded coiled coil is stabilized by one or more point mutations.
69. (New) The vaccine of claim 68, wherein the three-stranded coiled coil with one or more point mutations has SEQ ID NO:9.
70. (New) The vaccine of claim 62, wherein the three-stranded coiled coil is stabilized by chemical cross-linking.
71. (New) The vaccine of claim 62, wherein the gp41 monomers comprise SEQ ID NO:7.

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72. (New) The vaccine of claim 62, wherein the gp41 monomers comprise comprising SEQ ID NO:3 or SEQ ID NO:4.
73. (New) The vaccine of claim 71 or 72, wherein a stable three-stranded coiled coil formed from the gp41 monomers is stabilized by chemical cross-linking.
74. (New) The vaccine of claim 71 or 72, wherein a stable three-stranded coiled coil formed from the gp41 monomers is stabilized by one or more point mutations in one or more gp41 monomers.
75. (New) The vaccine of claim 62, further comprising a suitable adjuvant.
76. (New) A method of vaccinating an individual to prevent or treat infection by an enveloped virus, comprising: administering to the individual an immunogenically effective amount of a composition comprising the vaccine of claim 61.
77. (New) The method of claim 76, wherein the enveloped virus is an HIV1 virus or an HIV2 virus.
78. (New) The method of claim 76, wherein the vaccine is administered in combination with a physiologically acceptable carrier or diluent.
79. (New) The method of claim 76, wherein the carrier or diluent is sterile water or phosphate-buffered saline.
80. (New) The method of claim 76, wherein the vaccinating is performed to prevent or treat HIV infection or AIDS.

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81. (New) An antibody or binding portion thereof, raised against stabilized viral envelope protein comprising three parallel,  $\alpha$ -helical COOH-terminal viral envelope glycoprotein monomers that together form a stable three-stranded coiled coil having a conformation like that of a native form of the viral envelope glycoprotein when associated with a cellular membrane, wherein the stabilized viral envelope protein is substantially incapable of undergoing a conformational change to become active for membrane fusion, and wherein the monomer comprises SEQ ID NO:8.
82. (New) The antibody or binding portion thereof of claim 81, wherein the antibody or binding portion is polyclonal.
83. (New) The antibody or binding portion thereof of claim 81, wherein the antibody or binding portion thereof is produced by a hybridoma cell in culture.
84. (New) The antibody or binding portion thereof of claim 81, wherein the antibody or binding portion thereof is produced by an antibody-producing cell in a living organism.
85. (New) The antibody or binding portion thereof of claim 81, reactive with a native form of a HIV 1 or HIV 2 viral envelope glycoprotein.
86. (New) A method of detecting an enveloped virus in a sample comprising: exposing a sample to the antibody or binding portion thereof of claim 81, and identifying binding between the enveloped virus and the antibody or binding portion thereof.
87. (New) The method of claim 86, wherein the enveloped virus is HIV1 or HIV2.

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88. (New) A method of inhibiting infectivity of an HIV 1 or HIV 2 virus, comprising: contacting the HIV 1 or HIV 2 virus with an effective amount of the antibody or binding portion thereof of claim 81, under conditions effective for binding an antibody to the HIV 1 or HIV 2 virus.
89. (New) The method of claim 88, wherein said contacting comprises administering the antibody or binding portion thereof to a host before or following exposure of the host to HIV 1 or HIV 2 virus.
90. (New) A method for screening for drugs which can inhibit infection by an enveloped virus comprising:
- (a) providing a stabilized viral envelope protein comprising three parallel,  $\alpha$ -helical COOH-terminal viral envelope glycoprotein monomers that together form a stable three-stranded coiled coil having a conformation like that of a native form of the viral envelope glycoprotein when associated with a cellular membrane, wherein the stabilized viral envelope protein is substantially incapable of undergoing a conformational change to become active for membrane fusion, and wherein the monomer comprises SEQ ID NO:8;
- (b) exposing the stabilized viral envelope protein to a test compound; and
- (c) identifying whether the test compound binds to the stabilized viral envelope protein.
91. (New) The method according to claim 90, further comprising determining whether the binding affinity of gp120 for a complex of gp41 bound to the test compound is less than the binding affinity of gp120 for gp41.

Remarks

This Amendment and the above-referenced substitute SEQUENCE LISTING are filed in part to conform the above-referenced application to the requirements of 37 C.F.R. §§ 1.821 -